SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Irrigated Diagnostic/Ablation Catheter and accessories
Device Trade Names:	Biosense Webster NaviStar™/Celsius™ ThermoCool® Diagnostic/Ablation Deflectable Tip Catheters
Applicant's Name and Address:	Biosense Webster Inc. 3333 Diamond Canyon Road Diamond Bar, CA 91765
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P030031
Date of Notice of Approval to Applicant:	November 5, 2004

Device and Accessory Model Numbers:

Table 1 – List of Catheter Families and Models

Family Name	Model Number
NaviStar™ ThermoCool®	NS75T-BCT-252-HS
	NS75T-CCT-252-HS
	NS75T-DCT-252-HS
	NS75T-FCT-252-HS
	NS75TC-BCT-252-HS
	NS75TC-CCT-252-HS
	NS75TC-DCT-252-HS
	NS75TC-FCT-252-HS
Celsius™ ThermoCool®	D7IT-BL-252-RT
	D7IT-DL-252-RT
	D7IT-FL-252-RT
	D7ITC-BL-252-RT
	D7ITC-DL-252-RT
	D7ITC-FL-252-RT

Explanation of model numbers:

The NaviStar™ ThermoCool® catheters are available in the B, C, D, and F curves, and the Celsius™ ThermoCool® catheters are available in the B, D, and F curves, each being determined by the angle between the tip and shaft of the catheter, and by the radius of the

curve. Both catheter families are available with either a thermistor or thermocouple for sensing the tip temperature during an ablation procedure.

For the NaviStar™ ThermoCool® catheter, NS75T signifies the thermistor, and NS75TC signifies the thermocouple. Furthermore, the letter located after the "NS75T(C)-" in the model number signifies the type of curve for the catheter. For example, the NS75TC-FCT-252-HSI model has curve type F. Similarly, for the Celsius™ ThermoCool® catheter, D7IT signifies the thermistor, and D7ITC signifies the thermocouple; the letter located after the "D7IT(C)-" in the model number signifies the type of curve for the catheter.

Related Premarket Applications:

The NaviStar™ ThermoCool® catheter is derived from the NaviStar™ catheter approved under P990025 and the NaviStar™ DS catheter approved under P010068. The Celsius™ ThermoCool® catheter is derived from the Celsius™ catheter approved under P950005 and the Celsius™ DS catheter approved under P010068. The major modifications include a difference in tip electrode length (3.5 mm for Thermocool versus 4 and 8 mm) and addition of an internal irrigation lumen in the ThermoCool catheters. Wherever testing is not required in the present PMA, please refer to the SSEDs for previous PMAs for detailed information.

II. INDICATIONS FOR USE

The Biosense Webster NaviStar™/Celsius™ ThermoCool® Diagnostic/Ablation Deflectable Tip Catheters and related accessory devices are indicated for catheter-based cardiac electrophysiological mapping (stimulating and recording), and when used with the Stockert 70 generator, for the treatment of Type I atrial flutter in patients age 18 or older.

The NaviStar™ ThermoCool® catheter provides location information when used with the Carto EP/XP Navigation System.

III. CONTRAINDICATIONS

Do not use this device:

- in patients with active systemic infection; and
- if the patient has intracardiac mural thrombus or has had a ventriculotomy or atriotomy within the preceding four weeks.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the NaviStar™ ThermoCool® Diagnostic/Ablation Catheter instructions for use, the Celsius™ ThermoCool® Ablation Catheter instructions for use, and the Stockert 70 Radiofrequency Generator User Manual.

V. DEVICE DESCRIPTION

The device components which are the subject of the PMA are as follows:

A. NaviStar™ ThermoCool® Diagnostic/Ablation Deflectable Tip Catheters; and

B. Celsius™ ThermoCool® Diagnostic/Ablation Deflectable Tip Catheters.

Hereinafter, the two catheters are collectively referred to as the "ThermoCool catheter" unless otherwise specified.

For catheter ablation procedures, the ThermoCool catheter requires the use of the following:

- Stockert 70 RF Generator previously approved under P990071 and P010068;
- grounding pad (dispersive pad) previously approved under P990071;
- catheter interface cables (models D-1195 and D-1170) previously approved under P950005 and P990071; and
- a commercially available infusion pump that provides irrigation at rates indicated in the ThermoCool catheter instructions for use.

For additional aid in navigation, the NaviStar™ ThermoCool® catheter requires the use of these legally marketed devices:

- RefStar reference patch -- originally cleared under K954390 and K982415; and
- Carto EP/XP Navigation System -- originally cleared under K954395, K013083 and K020863.

Description

A. NaviStar™ ThermoCool® and Celsius™ ThermoCool® Diagnostic/Ablation Catheters

The NaviStar™ and Celsius™ ThermoCool® Diagnostic/Ablation catheters are two families of steerable, multi-electrode catheters with a deflectable tip.

The ThermoCool catheter is an electrophysiology electrode catheter with a 3.5-mm tip electrode, three ring electrodes, and a temperature sensor incorporated into the 7F deflectable tip. The tip electrode serves to deliver RF current from the RF generator to the desired

ablation site, and incorporates six small holes through which normal saline is passed for irrigation and cooling.

The tip electrode and ring electrodes are platinum-iridium with 2-5-2 spacing of the ring electrodes. The deflectable tip is extruded from polyurethane and is composed of three lumens. One lumen (0.022") contains a coil spring and a puller-wire, the second lumen (0.033") is used for irrigation, and the third lumen (0.036") contains the location sensor (for the NaviStar ThermoCool catheter only) and the lead wires.

The catheter body is single lumen high-torque 7.5F shaft for the NaviStar ThermoCool (the shaft diameter is 7 F for the Celsius ThermoCool) extruded from biocompatible PEBAX with a handpiece at the proximal end. A puller wire is anchored in the tip electrode and runs though the catheter shaft to a piston in the handpiece. A saline tube also extends from the tip through the shaft to an irrigation port on the handpiece. The irrigation port terminates in a standard luer fitting to permit the injection of normal saline to irrigate the tip electrode.

The usable length of the ThermoCool catheter is 115 centimeters. The catheter is provided sterile and for single patient use only.

B Differences between NaviStar™ and Celsius ThermoCool® Catheters

The NaviStar™ ThermoCool® catheter includes a location sensor, which consists of three orthogonally arranged sensor coils. The NaviStar™ ThermoCool® catheter is used with the Carto EP/XP Navigation System to generate catheter location and orientation information by interacting with a small alternating current (AC) magnetic field propagating from the location pad placed under the patient table. The Celsius does not include the location sensor.

In addition, the NaviStar™ ThermoCool® catheter features a 7F tip electrode, 8 F ring electrodes, and a 7.5 F shaft, whereas the Celsius™ ThermoCool® catheter features 7F tip electrode, ring electrodes and shaft.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Alternative therapy for Type I atrial flutter includes direct surgical ablation, RF catheter ablation with other approved diagnostic/ablation catheters, use of drugs for arrhythmia control, and antiarrhythmia pacing.

VII. MARKETING HISTORY

The NaviStar™ ThermoCool® and Celsius™ ThermoCool® Diagnostic/Ablation Catheters and accessories are have been marketed in Canada, Australia, China, Hong Kong, Singapore, Pakistan, Malaysia, Argentina, Brazil, Mexico, and the European Union since February 1999.

The NaviStar™ ThermoCool® and Celsius™ ThermoCool® catheter has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential Adverse Events associated with cardiac ablation for treatment of Type I atrial flutter include the following:

- Adult Respiratory Distress Syndrome (ARDS)
- Air embolism
- Anemia
- Anesthesia reaction
- Arrhythmias
- AV fistula
- Cardiac perforation/tamponade
- Cardiac thromboembolism
- Cerebrovascular accident (CVA)
- Chest pain/discomfort
- Complete heart block
- Component damage to ICD or implantable pacemaker
- Congestive heart failure
- Coronary artery spasm
- Death
- Dislodgement of implantable cardioverter defibrillator or permanent pacing leads
- Endocarditis
- Exacerbation of pre-existing atrial fibrillation
- Expressive aphasia
- Heart Failure
- Hemothorax
- Increased phosphokinase level
- Infections
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Local hematomas/ecchymosis
- Myocardial infarction
- Obstruction or perforation or damage to the vascular system
- Pericardial effusion
- Pericarditis
- Phrenic nerve damage
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Respiratory Depression
- Seizure
- Temporary complete heart block
- Thrombi
- Thromboembolism
- Transient ischemic attack (TIA)
- Unintended (in)complete AV, sinus node or other heart block or damage
- Valvular damage/insufficiency
- Vascular bleeding
- Vasovagal reactions
- Volume overload
- Ventricular tachycardia
- Worsening chronic obstructive pulmonary disease

For actual adverse events observed during the clinical study (within 7 days post-ablation), please refer to Table 16.

IX. SUMMARY OF PRECLINICAL STUDIES

The sponsor conducted preclinical and animal studies on the NaviStar™ and Celsius™ ThermoCool® catheters. These tests are summarized below.

In the tests described below, the catheters were single-sterilized prior to testing. Visual examinations noted below were conducted using a microscope.

A. NaviStar™ ThermoCool® Catheter

A.1. – Mechanical Performance of the NaviStar™ ThermoCool® Catheter

The sponsor performed mechanical testing involving the NaviStar™ ThermoCool catheter. Except for the deflection test, the catheters were soaked for 5 hours in a 37° C saline bath prior to testing. Table 2 summarizes the mechanical performance testing involving the NaviStar™ ThermoCool® catheter. Besides one sample that did not pass the deflection test, all remaining test samples met the established acceptance criteria for mechanical performance testing.

Table 2 - Mechanical Testing of NaviStar™ ThermoCool® Catheter

Test	Sample Size	Acceptance Criteria	Results*
Deflection	30	No mechanical failures before 50 cycles	passed with deviation**
Gas pressure/joint seal	30	No leaks under 4.6 psi	passed
Pull force of full length catheter	15	No failure before 4 lbs	passed
Pull force of irrigation lumen extension	15	No failure before 4 lbs	passed
Entire catheter torque	15	No failure before 1 in and 2 turns	passed

* In documenting results, "passed" means that all samples passed.

** One sample failed after 28 deflection cycles. Failure investigation identified the root cause as an assembly error. Omitting the sample which failed due to an assembly error, 29 devices passed with 0 failures, meeting the requirement of 95% confidence and 90% reliability.

Tests not conducted

The main differences between the NaviStar™ ThermoCool® catheter in this PMA and NaviStar™ catheter approved under P990025 and the NaviStar™ DS catheter approved under P010068 are the length of the tip electrodes and the additional lumen for irrigation. Due to these similarities, the following mechanical tests were not repeated in this PMA:

- Torque Barrel to Connector
- Torque Plot
- Pull Test Barrel to Connector
- Pull Test Shaft to Piston Joint

A.2. - Electrical Performance of the NaviStar™ ThermoCool® Catheter

Electrical performance testing was conducted on catheters sterilized prior to the qualification test (pre- and post-simulated ablation) to evaluate whether electrical

performance was compromised during the test cycle. Table 3 summarizes the electrical performance testing involving the NaviStar™ ThermoCool® catheter. All test samples met the established acceptance criteria for electrical performance testing.

Table 3 - Electrical Performance Testing of NaviStar™ ThermoCool Catheters

Test	Sample Size	Acceptance Criteria	Results
DC Lead Resistance	30	<10 Ω	passed
DC Leakage Current	30	< 1μAmp	passed
RF Lead Impedance @ 5 kHz	30	<10 Ω	passed
RF Lead Impedance @ 500 kHz	30	<25 Ω	passed
RF Isolation Impedance @ 5 kHz	30	>100 kΩ	passed
RF Isolation Impedance @ 500 kHz	30	>1 kΩ	passed
Temperature Accuracy (idle)	30	37 ± 2°C and 60 ± 2°C	passed
Verify Calibration	30	Calibration results read "OK"	passed

One note is that the temperature accuracy of the NaviStar catheter used in the present study has a margin of error of +/- 5 degrees C, while the usual accuracy for other catheters is +/- 3 degrees C. The larger margin of error is acceptable since the NaviStar and Celsius ThermoCool Catheters are used with the Stockert RF generator operating in the power control mode, so that temperature accuracy is less needed. This margin of error is indicated in the ThermoCool catheter labeling.

A.3. - Simulated Use of NaviStar™ ThermoCool® catheter

Functional performance testing and simulated use testing involving the NaviStar™ ThermoCool® catheter are summarized in Table 4. Besides one sample that did not pass the deflection test as mentioned in Table 2, all remaining test samples met the established acceptance criteria for functional performance testing.

Table 4 – Functional Performance Testing of NaviStar™ ThermoCool

Test	Sample Size	Acceptance Criteria	Results
Catheter soak test	30	No anomalies or defects after soaking at 37^0C for $\geq$ 5 hours	passed
Steering through vascular model	30	No deformation, kink and/or electrode detachment after 10 insertions	Passed
Tip side load (5 runs)	30	Force required to bend tip 90 degrees > 4 grams	Passed
In bath rotation and deflection (100 times)	30	No mechanical failure	passed with deviation*
Catheter flow rate	30	28.5 – 34.5 ml	Passed
Ablation test – 10 burns**	30	Consistent lesions should be created	Passed

* All units passed except one sample, which failed the deflection test (see Table 2).
** Simulated use ablation using a beef heart in a 37°C saline bath was conducted to evaluate the functional performance of the catheter and accessories.

A.4. - Electromagnetic Compatibility of NaviStar™ ThermoCool® catheter
Electromagnetic compatibility (EMC) testing was conducted on the NaviStar™ ThermoCool® catheter, as part of an integrated system test with the CARTO System, Stockert generator and CoolFlow pump.

One note is that the EMC tests are considered passing based on the premise that the device is intended for use inside an X-ray shielded room, in order to reduce the acceptance level. This restriction in locating the device is now reflected in the labeling. The affected test results concerned radiated immunity level and radiated emissions.

A.5. - Electrical Safety of NaviStar™ ThermoCool® catheter
Electrical safety testing was tested on 30 catheters:
Sterilization, aging, simulated shipping and simulated use (soak, steering, side load, repeated deflection, irrigation flow, RF ablation), followed by DC leakage test (less than 1.0 microampere between wires at 300 V).

A.6. - Biocompatibility and Sterilization of NaviStar™ ThermoCool® catheter
Biocompatibility - Since the NaviStar™ ThermoCool catheter and the NaviStar™ 4 mm catheter approved under P990025 have the same patient contacting materials, biocompatibility was not re-validated, except for the polyimide tubing used inside ThermoCool catheter to deliver saline to the patient. The biocompatibility tests for the polyimide tube are the following (all tested samples passed):

ISO MEM elution using L-929 mouse fibroblast cells
ISO intracutaneous reactivity test
USP acute systemic injection test
Hemolysis test (NIH method) -- Direct contact method
Partial thromboplastin time (PTT)
Platelet & leukocyte counts
Complement activation C3a and SC5b-9 assay
ISO Guinea pig maximization sensitization test method
Thrombogenicity test

Sterilization – The devices are sterilized by ethylene oxide, using the same methods as the NaviStar™ 4 mm catheter approved under P990025.

Table 5 lists the patient and user contacting materials that were tested in accordance with ISO 10993 and submitted under P990025. All materials are classified as short duration, direct blood path, and externally communicating per ISO 10993-1.

Table 5 - Patient Contacting Materials of the ThermoCool Catheter

Material Spec No.	Component	Material Description
M-5439-03	Deflectable Tip	55D Pellethane
M-5013-04 M-5203-111	Ring and Tip Electrodes	90%/10% Platinum/Iridium
M-5439-05	Flexible Shaft	75D Pellethane
P-9749-03	Sensor Housing	Polyetherether ketone
P-9231	Shaft to Tip Adhesive	Polyurethane

A.7. - ThermoCool® Catheter Upper Allowable RF Application Limit

A study was conducted using a beef heart (non-beating) in a 37 °C saline bath to determine the upper allowable lesion limits for the NaviStar™ ThermoCool® catheter. Thirty (30) catheters were tested for a total of 250 minute burn duration each in order to assure that 125 lesions, given for 120 second each, could be delivered safely and effectively. Ablation was followed by a full suite of mechanical and electrical testing. Based on the evaluation of the first five and last five lesions, the functionality of the catheter remained the same before and after the 125 lesions. Thus, the test results support the sponsor's ability to label the catheter for up to 125 two-minute applications.

A.8. - Animal Data of NaviStar™ ThermoCool® Catheter

The sponsor provided five animal studies in the canine model as verification of proof-of-principle, as summarized below:

Study One (11 canines)

The conclusion of this study was that saline irrigation maintains a low electrode-tissue interface temperature during radiofrequency application at high power, preventing an impedance rise and allowing for deeper and larger lesions.

Concern (for Study One)
It was noted in 6/75 applications (8%) that an abrupt impedance rise with an audible pop and without coagulum occurred. The sponsor attributed this finding to steam release from below the surface, likely related to superheating of the tissue and subsequent steam formation. In addition, it was noted that tissue temperatures during radiofrequency ablation with saline irrigation were significantly higher than in the non-irrigated catheter ablation treatment groups.

To resolve this issue, the sponsor has adopted the following controls in the use of the ThermoCool catheter:

* Use power titration, and an irrigation scheme consistent with applied power.

* Limit maximum power with orientation: Power not to exceed 50 W when the catheter is parallel to the tissue and 35 W if the catheter is perpendicular to the tissue.

* Each RF application will not exceed 120 seconds in duration.

Study Two (11 canines)
In this study, lesion size was found to be significantly smaller for the 5 mm tip electrode compared to the 3.5 mm tip. The number of steam pops was found to be higher in the 4 mm conventional catheter compared to the irrigated catheter.

Study Three (11 canines)
In this study, smaller electrode sizes (2 mm vs. 5 mm) resulted in the transmission of a greater fraction of the radiofrequency power to the tissue and resulted in higher tissue temperature and larger lesions.

Study Four (5 canines)
In this study, an irrigation flow rate of 30 cc/min was found to be adequate to prevent an impedance rise and char (coagulum) formation for RF applications at 50 watts. At lower flow rates, impedance rises and coagulum formation was noted.

Study Five (11 canines)
The study results demonstrated that lower saline irrigation rates (10-30 cc/min) are sufficient to prevent an impedance rise and coagulum formation for applications of radiofrequency current at 30 watts for 60 seconds. For higher energy application (50 watts), an irrigation flow rates of 30 cc/min was adequate in preventing the incidence of impedance rise.

A.9. - Shelf Life of NaviStar™ ThermoCool® Catheter
The NaviStar™ ThermoCool® Catheter is validated for a one year shelf life, as follows:

The NaviStar ThermoCool catheter is packaged in a straight configuration in a single package while the Celsius ThermoCool catheter is double pouched in a round configuration. The sponsor exposed the packaging to 3x EtO during packaging validation. Packages were aged adequately for 26.2 days when stored at 60°C, or 38°C above ambient temperature.

Both Bubble Leak (in accordance with ASTM F2096) and Peel Strength tests were performed at one year for both packages. Sample size for each test ran between 30 and 60 packaged products each (packages were not used for more than one test type). Simulated shipping tests were performed in accordance with the International Safe Transit Association (ISTA) shipping protocols.

After storage, the catheters were run through mechanical and electrical tests, including ablations. Only one out of 30 catheters failed. Tests for one year have been completed, and 3 year tests are ongoing.

B. Celsius™ ThermoCool® Catheter

The Celsius™ ThermoCool® catheter is claimed to be functionally equivalent to the NaviStar™ ThermoCool® catheter in most aspects, with the exception that the NaviStar™ ThermoCool® catheter has the additional ability to interface with a mapping system (CARTO EP/XP) and map the target areas of the heart. Design differences between the two catheter families are predominantly the result of the need to accommodate additional electrical connections and navigation electrodes. The therapeutic modality for both catheters is identical. The Celsius™ catheter is essentially a simplified version of the NaviStar™ Catheter.

In addition, the Celsius™ ThermoCool® catheter is similar to the Celsius™ catheter approved under P950005 and the Celsius™ DS catheter approved under P010068. As a result, many tests performed on the NaviStar™ ThermoCool® catheter (described above), and previously conducted on the Celsius™ Catheter (reference P950005) or Celsius™ DS catheter are not repeated on the Celsius™ ThermoCool® catheter.

The verification test results for the Celsius™ ThermoCool® catheter are summarized below:

B.1. – Mechanical Performance of the Celsius™ ThermoCool® catheter

The sponsor performed mechanical testing for the Celsius™ ThermoCool catheter. Except for the deflection test, the catheters were soaked for 5 hours in a 37° C saline bath prior to testing. Table 6 summarizes the mechanical performance testing involving the Celsius™ ThermoCool® catheter. Besides two samples that did not pass the deflection test, all remaining test samples met the established acceptance criteria for mechanical performance testing.

Table 6 - Mechanical Testing of Celsius™ ThermoCool® Catheters

Test	Sample Size	Acceptance Criteria	Results*
Deflection	33	No mechanical failures before 50 cycles	pass with deviation**
Gas pressure/joint seal	33	No leaks under 4.6 psi	Passed
Pull force of full length catheter	17	No failure before 4 lbs	Passed
Pull force of irrigation lumen extension	17	No failure before 4 lbs	Passed
Entire catheter torque	17	No failure before 1 in-oz and 2 turns	Passed

* In documenting results, "passed" means that all samples passed.
** Two samples failed with less than 50 deflection cycles. Failure investigation identified the root cause as an assembly error. Omitting the samples which failed due to an assembly error, 31 devices passed with 0 failures, meeting the requirement of 95% confidence and 90% reliability.

B.2. - Electrical Performance of the Celsius™ ThermoCool® catheter

Electrical performance testing was conducted on catheters sterilized prior to the qualification test (pre- and post-simulated ablation) to evaluate whether electrical performance was compromised during the test cycle. Table 7 summarizes the electrical performance testing involving the Celsius™ ThermoCool® catheter. All test samples met the established acceptance criteria for electrical performance testing.

Table 7 - Electrical Performance Testing of Celsius™ ThermoCool® Catheters

Test	Sample Size	Acceptance Criteria	Results
DC Lead Resistance	33	<10 Ω	Passed
DC Leakage Current	33	< 1μAmp	Passed
RF Lead Impedance @ 5 kHz	33	<10 Ω	Passed
RF Lead Impedance @ 500 kHz	33	<25 Ω	Passed
RF Isolation Impedance @ 5 kHz	33	>100 kΩ	Passed
RF Isolation Impedance @ 500 kHz	33	>1 kΩ	Passed
Temperature Accuracy (idle)	33	37 ± 2°C and 60 ± 2°C	Passed

B.3. – Simulated Use of the Celsius™ ThermoCool® catheter

Functional performance testing and simulated use testing of the Celsius™ ThermoCool® catheter are summarized in Table 8. All test samples met the established

acceptance criteria for functional performance testing, except that the test used an 8 F introducer. This compatibility to an 8 F introducer is now indicated in the labeling.

Table 8 – Functional Performance Testing of Celsius™ ThermoCool® Catheters

Test	Sample Size	Acceptance Criteria	Results
Catheter soak test	33	No anomalies or defects after soaking at 37° C for > 5 hours	Passed
Steering through vascular model	33	No deformation, kink and/or electrode detachment after 10 insertions	Passed
Tip side load (5 runs)	33	Force required to bend tip 90 degrees > 4 grams	Passed
In bath rotation and deflection (100 times)	31*	No mechanical failure	Passed
Catheter flow rate	33	28.5 – 34.5 ml	Passed
Ablation test – 10 burns**	33	Consistent lesions should be created	Passed

* Two units that failed the deflection test were excluded from this test.
** Simulated use ablation using a beef heart in a 37°C saline bath was conducted to evaluate the functional performance of the catheter and accessories.

B.4. - Electromagnetic Compatibility of Celsius™ ThermoCool® catheter
Electromagnetic compatibility (EMC) testing was not conducted on the Celsius™ ThermoCool® catheter, due to similarity with the NaviStar™ 4 mm catheter approved under P990025.

B.5. - Electrical Safety of Celsius™ ThermoCool® catheter
Electrical safety testing was tested on 33 catheters:
Sterilization, aging, simulated shipping and simulated use (soak, steering, side load, repeated deflection, irrigation flow, RF ablation), followed by DC leakage test (less than 1.0 microampere between wires at 300 V).

B.6. - Animal Testing of Celsius™ ThermoCool® catheter
Due to the similarity of the Celsius™ ThermoCool® with the NaviStar™ ThermoCool® catheter, no animal testing was performed on the Celsius™ ThermoCool® catheter.

B.7. - Shelf Life of Celsius™ ThermoCool® catheter
The Celsius™ ThermoCool® Catheter is approved for a one year shelf life, based on similarity to the NaviStar ThermoCool catheter.

X. SUMMARY OF CLINICAL STUDIES

The clinical testing described below was performed with the NaviStar™ ThermoCool® catheter, and not with the Celsius™ ThermoCool® catheter. Since the ablation capabilities of both NaviStar™ and Celsius™ ThermoCool® catheters were shown with pre-clinical testing to be similar, clinical testing results from the NaviStar™ ThermoCool® study, as reported below, may be extrapolated to what would be expected when using the Celsius™ ThermoCool® catheter.

A. Objective

The objective of the study was to determine if the NaviStar™ ThermoCool® catheter, when used in conjunction with Carto™ EP/XP Navigation System, Stockert 70 RF Generator and related accessories, is safe and effective for the treatment of Type I atrial flutter in patients age 18 or older.

B. Study Design

The study was a prospective, non-randomized, unblinded, multi-center study conducted at 22 investigational sites (21 sites in US; 1 in Canada).

B.1. - Study Endpoints:

The endpoints for the study were as follows:

- **procedural safety** – defined by the absence of serious complication associated with the use of the investigational device within seven days of the ablation procedure; and

- **acute procedural success** – defined as complete bi-directional conduction block (BDB) across the isthmus, and the inability to induce Type I atrial flutter post-procedure.

Long-term freedom from atrial flutter recurrence was not specifically identified as a study endpoint. Instead, acute procedural success was used as a surrogate endpoint for this parameter. Long-term (defined as 6 months post-treatment) freedom from atrial flutter recurrence information was also collected, in order to enable FDA to assess whether the surrogate endpoint was reasonable.

B.2. - Objective Performance Criteria (OPC):

Objective performance criteria (OPC) were prospectively established. The OPC for the safety endpoint used for this study was derived from the FDA guidance document "Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Guidance for Industry, July 2002 1998 NASPE Registry." The OPC for the effectiveness endpoint was based on an extensive literature search involving acute success rates associated with radiofrequency ablation of atrial flutter. The OPCs are defined below:

- **Safety**: major adverse events within 7 days of the procedure occur at a rate of **2.7%** or less with a **7%** one-sided 95% upper confidence bound;

- **Acute success**: **88%** with an **80%** one-sided 95% lower confidence bound.

B.3. - Subject Accountability

The table below documents the accountability and disposition of enrolled subjects.

Table 9 - Subject Accountability and Disposition

Subjects enrolled in study	198
Subjects not ablated with the NaviStar ThermoCool catheter	8
Excluded Subjects - enrolled but in whom the investigational catheter was not inserted	3
Discontinued Subjects - either (1) in whom the investigational catheter was inserted but did not receive RF energy because of non-investigational equipment failure, or (2) for whom the arrhythmia was determined to be non-study arrhythmia at the time of electrophysiologic study (e.g., atypical atrial flutter).	5
Subjects ablated with NaviStar ThermoCool catheter	190
Subjects ablated with NaviStar ThermoCool catheter and non-investigational catheter*	19
Subjects ablated **only** with NaviStar ThermoCool catheter	171
Subjects in whom BDB was not assessable	4

* This category includes enrolled subjects who received ablation therapy with the investigational catheter at the start of the procedure and for whom the investigator then switched to a non-protocol catheter to complete the procedure. Further, subjects who could not receive ablation due to investigational device failure are included in this category. These subjects were considered acute effectiveness failures.

Effectiveness Analysis Population (n=190) was defined as all subjects who received ablation therapy with the investigational catheter and for whom a valid assessment of BDB at the acute endpoint could be made OR if 6 month follow-up data were available.

Safety Analysis Population (n=190) was defined as all enrolled subjects in whom the investigational catheter was inserted and received ablation therapy. Additionally, the rate of major adverse events is also reported for subjects in whom the investigational catheter was inserted and used for either mapping and/or ablation and for discontinued subjects. This additional category is referred to as the Inserted Patient Cohort (n=195).

B.4. - Subject Demographics

The table below summarizes the demographic information of all study subjects who received ablation therapy.

Table 10 – Subject Demographics
(All Subjects who Received Ablation Therapy - n=190)

Gender	N	%
Female	44	23.2
Male	146	76.8
Age (years)		
Mean ± standard deviation	59.8 ± 12.6	
Range	18-90	

Additionally, for the Inserted Patient Cohort of 195 subjects, 72 subjects (36.9%) did not have a concomitant arrhythmia reported in addition to Type I atrial flutter. One-hundred and sixty-five (165) concomitant arrhythmias were reported for 123 subjects. The most common concomitant arrhythmias were atrial fibrillation (n=104) and atypical atrial flutter (n=27).

C. Results

C.1. - Intraprocedural Data
Tables 10 and 11 describe the procedural data.

Twenty-eight (28) subjects received ablation therapy for an arrhythmia other than Type I atrial flutter during the same index ablation procedure. The additional arrhythmias ablated were: 14 atrial fibrillation, 9 atrial tachycardia, 3 AVNRT, 1 intra-atrial tachycardia, 1 non-isthmus atrial flutter and 1 macro-reentry around the SVC eustachian ridge. One subject had more than one concomitant arrhythmia ablated.

Table 11 - Power, Temperature and Impedance Data

Description	**Mean ± Standard Deviation**	**Range**
# RF applications/procedure[1] (n=188 procedures)	19 ± 16	1-86
Total saline infused by ThermoCool Catheter (ml)[2] (n=169 procedures)	999.7 ± 605.5	60-3750
Maximum power (Watts)/application[3] (n=3502 RF applications)	35.0 ± 9.5	2-59
Maximum temperature (°C)/application[3] (n=3476 RF applications)	39.6 ± 5.1	14-87
Maximum impedance (Ohms)/application[3] (n=3431 RF applications)	112.1 ± 21.0	13-251

[1] One subject had missing RF information; one subject did not undergo ablation with the NaviStar ThermoCool catheter.
[2] Some procedural data are missing.
[3] Power, temperature, and impedance not documented for several RF applications.

Table 12 – Overall Fluoroscopy/Procedure Time (minutes)

Description	Mean ± Standard Deviation	Range
Total fluoroscopy time/procedure[1] (n=189 procedures)	50.2 ± 32.4	8-174
Total procedure time[1] (n=190 procedures)	341.6 ± 166.9 (5.7±2.8 hours)	96-925
Total fluoroscopy time/procedure for subjects with additional rhythms ablated during index procedure (n= 28 procedures)	58.8 ± 24.7	18-115
Total fluoroscopy time/procedure for subjects without concomitant ablation (n=161 procedures)	48.7 ± 33.4	8- 174
Total procedure time for subjects with additional rhythms ablated during index procedure (n= 28 procedures)	503.8±193.0 (8.4±3.2 hours)	158-804
Total procedure time for subjects without concomitant ablation (n= 162 procedures)	313.5±145.2 (5.1±2.4 hours)	96-925

[1]Incomplete fluoroscopy time was reported for one (1) subject and incomplete procedure time was reported for one (1) subject.

C.2. - Acute Procedural Success

Acute success, defined as complete bi-directional conduction block across the isthmus at a minimum of 60 minutes following application of the last RF application, was analyzed. Acute success evaluation was based on the Efficacy Population, which was defined as all subjects who received ablation therapy with the investigational catheter and in whom a valid assessment of BDB could be made (n = 190 - 4 = 186).

Table 13 describes the acute ablation outcomes.

Table 13 - Acute Ablation Outcomes (n=186)

	# Success / # Subjects Ablated	Percentage (one-sided 95% confidence bound)
Acute Study Results	159/186	85% (81%)
OPC		88% (80%)

C.3. – Composite Assessment of Atrial Flutter Ablation Success

As noted in the above section, 159 subjects had BDB confirmed acutely after the ablation procedure.

In addition, of the four subjects in whom BDB was not measured acutely after the ablation procedure, 3 subjects were free of recurrence of atrial flutter at 6 months follow-up and one could not be validated. For the composite assessment, the 3 subjects were considered a success and the 1 subject a failure. Table 14 summarizes the composite results.

Table 14 – Composite Assessment of Atrial Flutter Success

	# Success / # Subjects Ablated	Percentage (one-sided 95% confidence bound)
Study Results	162/190	85.3% (80.2%)
OPC		88% (80%)

C.4. - Freedom from Type I Atrial Flutter Recurrence at Six-Month Follow-Up

As indicated in section B.1 above, long-term freedom from atrial flutter recurrence was not a study endpoint. The long-term results are presented here in order to assess the suitability of the surrogate endpoint BDB.

Freedom from Type I atrial flutter recurrence was evaluated in subjects in whom BDB was achieved (as measured acutely) and for whom 6-month post-ablation information was available. Based on these criteria, information was available on a total of 147 subjects. Results are described in the table below.

Table 15 - Freedom from Type I atrial flutter at 6 months (Results based on 147 subjects)

Description	N	Percent
Subjects in whom BDB was achieved acutely and for whom 6-month information was available	147	100%
Subjects free from recurrence	136	93%
Subjects free from recurrence and anti-arrhythmic drug change	118	80%
Subjects with recurrence of atrial flutter	11	
Subjects with AAD changes to treat atrial fibrillation	15	
Subjects with AAD changes to treat atrial or supraventricular tachycardias	3	

These results provide reasonable evidence that acute procedural success serves as an appropriate surrogate for long-term freedom from atrial flutter recurrence.

C.5. - Adverse Events

A major adverse event was defined as any clinical event that occurred within seven days post-ablation and which resulted in (1) death, (2) a life-threatening complication, or (3) a persistent or significant disability/incapacity that required inpatient hospitalization or prolonged hospitalization or required intervention to prevent a permanent impairment of a body function or damage to a body structure. A minor adverse event was defined as any adverse event resulting in minimal transient impairment of a body function or damage to a body structure, or which did not require any intervention other than monitoring or events occurring more than 7 days post-ablation.

Major Adverse Events

Of the 190 subjects who received ablation therapy with the investigational catheter, 33 major adverse events were reported in 30 subjects. The overall percentage of subjects who experienced a major adverse event was 15.8%. The one-sided 95% confidence bound rate was 20.9%. For subjects who had the investigational catheter inserted and used for mapping and/or ablation (n = 195), the major adverse event rate was 15.4%, and the one-sided 95% confidence bound rate was 20.4%. Table 16 summarizes the major adverse events.

Table 16 - Major Adverse Events observed within 7 days post-ablation

Total Number Subjects with a Major AE n=30
Cardiovascular total = 15 subjects
Arrhythmia complications = 5 subjects
complete atrioventricular block during procedure
bradycardia requiring pacemaker implant
ventricular tachycardia
atrial fibrillation
atrial fibrillation & atypical atrial flutter
Pericardial effusion/tamponade = 4 subjects
pericardial tamponade
pericardial tamponade after mapping only
pericarditis with effusion
RA thrombus, LV thrombus and pericardial effusion
Intracardiac thrombus = 2 subjects
RAA thrombus
RA thrombus, LV thrombus and pericardial effusion
myocardial infarction = 1 subject
congestive heart failure = 4 subjects
pedal edema
dyspnea, rales requiring furosemide
dyspnea treated with one dose furosemide
pulmonary edema by PE treated with one dose furosemide

Pulmonary acute respiratory distress syndrome = 2 subjects aspiration pneumonia = 2 subjects pneumonia = 3 subjects asthma = 1 subject	total = 8 subjects
Anesthesia related sedation induced apnea (intubation not required) sedation induced co2 retention with lethargy (intubation not required)	total = 2 subjects
Vascular arteriovenous fistula/femoral artery-saphenous vein pseudoaneurysm/right femoral artery	total = 2 subjects
Urologic urinary tract infection urinary retention	total = 2 subjects
Cholecystitis	1 subject
Neurologic parkinson's disease transient extremity numbness/possible tia	2 subjects

* Note: Some subjects are listed more than once in the above table.

Three subjects died during the course of the study. One subject died due to cardiac arrest caused by cardiomyopathy and chronic obstructive pulmonary disease (COPD) complications 11 days post-ablation, one subject died following pulmonary valve replacement surgery 2 months post-ablation, and the third death was due to lung cancer more than 2 years following the ablation procedure. All deaths were determined to be unrelated to the procedure and device.

An overall risk benefit evaluation of these adverse events was performed and a detailed review of each adverse event was completed. The adverse event rate described above was assessed to be specifically correlated to (1) the concomitant ablation procedures performed during the index procedure and (2) the increased number of co-morbid conditions present in the subject population enrolled relative to patient population from which the OPCs were derived. See section C.1 for a list of concomitant ablation procedures.

C.6. - Statistical Analysis

Table 17 summarizes the safety and effectiveness of the device when compared to the control group OPC established for safety and acute success.

Table 17 - Comparison of Endpoints between NaviStar™ ThermoCool Study and OPC

Endpoint	OPC		NaviStar™ ThermoCool Study	
	%	One-sided 95% Confidence Bound	% (N)	One-sided 95% Confidence Bound
Acute Success	88%	80%	85.3% (162/190)	80.2% (Lower bound)
Major Complications	2.7%	7%	15.8% (30/190)	20.9% (upper bound)

With comparison of the lower bounds of the acute success endpoints (80.2% vs. 80%), the results demonstrate that the NaviStar™ ThermoCool catheter met the OPC for acute success. As previously explained in section C.5, although the device exceeded the upper bound of major complications, review of the specific events showed that they were related to the concomitant ablation procedures performed in addition to atrial flutter ablation and the subject population co-morbid conditions. Accordingly, study results demonstrate a reasonable assurance of the safety profile of the device.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Pre-clinical testing demonstrates that the NaviStar™ ThermoCool® catheter, Celsius™ ThermoCool® catheter and accessories (Stockert 70 RF generator, cables and junction box) will maintain mechanical and electrical integrity under the proposed conditions of use. Additionally, biocompatibility testing of the patient-contacting materials demonstrates that the devices are biocompatible under the proposed conditions of use.

Clinical testing and analysis demonstrate that the NaviStar™ ThermoCool® and Celsius™ ThermoCool® catheters when used with the Stockert 70 RF generator are reasonably safe and effective for the treatment of Type I atrial flutter.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA is similar to information previously reviewed by this panel.

XIII. CDRH DECISION

CDRH issued an approval order on November 5, 2004.

The applicant's manufacturing facilities were inspected on March 20, 2003 and found to be in compliance with the device Quality System Regulation (Part 820). Hence, no new inspection is needed.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.

Post-approval Requirements and Restrictions: See approval order.